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Original Research Paper

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TO STUDY THE EFFECTS OF 0.25 MG SINGLE DOSE OF PALONOSETRON, GIVEN INTRAVENOUSLY, ON ACUTE AND DELAYED CHEMOTHERAPY INDUCED NAUSEA AND VOMITING

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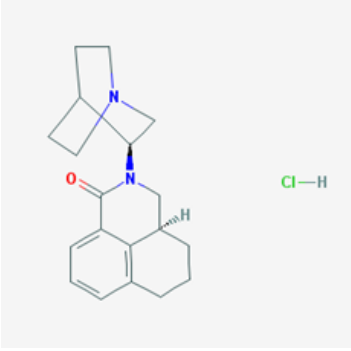
ABSTRACT This study aimed at reporting efficacy and tolerability of palonosetron, a second generation 5-HT3 receptor antagonist in preventing acute and delayed chemotherapy induced nausea and vomiting (CINV). 50 adult cancer patients received single i.v. dose of palonosetron 0.25 mg, 30 min before initiation of chemotherapy. The primary end point was proportion of patients with no emetic episodes and no rescue medication within 24 hours after chemotherapy completion (acute period). Secondary end point included efficacy in preventing delayed CINV (24-48 hours post-chemotherapy). The study showed that only 2 out of 50 patients had vomiting within 24 hours post chemotherapy completion, and none of the patients had nausea even after 48 hours post chemotherapy. Thus proving that efficacy of palonosetron is more for delayed CINV than for acute CINV.

KEYWORDS : Palonosetron, CINV, Efficacy.

Introduction:[1]

Palonosetron Hydrochloride is the hydrochloride salt of palonosetron, a carbazole derivative and a selective serotonin receptor antagonist with antiemetic activity. Palonosetron competitively blocks the action of serotonin at 5-hydroxytry ptamine type 3 (5-HT3) receptors located on vagal afferents in the chemoreceptor trigger zone (CTZ), resulting in suppression of chemotherapy-induced nausea and vomiting. The CTZ is located in the area postrema on the dorsal surface of the medulla oblongata at the caudal end of the fourth ventricle and outside the blood-brain barrier (BBB).

2D structure: Figure 1:



Palonosetron is a highly potent, selective, second-generation 5-HT3 receptor antagonist with a 5-HT3 receptor binding affinity that is ~100-fold higher than other 5-HT3 receptor antagonist counterparts like granisetron, ondansetron. Palonosetron also has an extended plasma elimination half-life of ~40 h [15], significantly longer than others in its class – ondansetron (4hrs), granisetron (8.9 hrs).

In this study, efficacy of palonosetron, to prevent acute and delayed chemotherapy induced nausea and vomiting has been studied.

Aim and objectives:

To study the effects of 0.25 mg single dose of Palonosetron, given intravenously, on acute and delayed chemotherapy induced nausea and vomiting.

Materials and methods:

This study is a retrospective type of study with data maintained prospectively. The study included 50 patients who were administered chemotherapy for histologically or cytologically confirmed malignant disease. The patients in this study had carcinoma esophagus, breast carcinoma or carcinoma colon. Every patient was given a single dose of 0.25 mg palonosetron, intravenously prior to starting chemotherapy. Since the patients included in this study were of CA esophagus, CA breast and CA colon, the chemotherapy consisted of drugs like cyclophospha mide, cisplatin, doxorubicin, 5 fluorouracil which have proven emetogenic properties.

Acute onset chemotherapy induced nausea and vomiting (CINV) was considered in this study as nausea and vomiting occurring immediately within 24 hrs of completion of chemotherapy. Delayed onset CINV was considered as nausea and vomiting occurring after 24 hrs of chemotherapy completion.

Once the drug was administered and the chemotherapy was completed, all the patients were evaluated to see for chemotherapy induced nausea and vomiting as well as to evaluate the other side effects of palonosetron like headache, constipation, dizziness, generalized weakness and ECG changes.[2][3][4] The patients were evaluated for the next 48 hours after the completion of chemotherapy.

Inclusion criteria:

- Age- > 30 years
- Histologically or cytologically confirmed malignant disease.

(CA Colon, CA Breast, CA Esophagus)

Exclusion criteria:

- Patients were excluded if they were unable to understand or cooperate with the study procedure,
- Patients having carcinoma other than breast, esophagus and colon,
- Taking any other antiemetic drug or any steroids prior to the treatment,
- Patients requiring radiation treatment.

Results

Table 1: The demographic characteristics of cases studied (n=50).

Parameters	Statistics
Age (Mean ± SD)	50.2 years ± 5.9 years
Age Range	Min: 30 years, Max: 65 years
Sex	Male : 22, Female : 28

Sex Ratio (Male to Female)	0.78 : 1.00
Indications of chemotherapy	CA Colon : 12 (24.0%)
	CA Breast : 28 (56.0%)
	CA Esophagus : 10 (20.0%)

Table 2: The distribution of incidence of complications (n=50).

Complications	0-24Hrs (Immediate)	After 24-Hrs (Delayed)
Nausea	5 (10%)	0
Vomiting	4 (8%)	2 (4%)
Headache	5 (10.0%)	2 (4.0%)
Constipation	6 (12.0%)	5 (10.0%)
Dizziness	4 (8.0%)	6 (12.0%)
Generalized weakness	2 (4.0%)	2 (4.0%)
ECG Changes	0	0

Of 50 cases studied, 5 cases (10%) had nausea immediately within 24 hours of completing the chemotherapy (immediate) and none of the patients had nausea after 24 hoursof completion of chemotherapy (delayed). Vomiting was seen as an immediate side effect in 4 cases (8%) and as a delayed effect in 2 cases (4%). Five cases (10.0%) had headache as an immediate side effect and 2 cases (4.0%) had it as a delayed effect. The other complications such as constipation, dizziness and generalized weakness was present in 6 cases (12.0%), 4 cases (8.0%) and 2 cases (4.0%) within 24 hours of completing the chemotherapy respectively. Constipation, dizziness and generalized weakness were seen in 5 cases (10.0%), 6 cases (12.0%) and 2 cases (4.0%) respectively after 24 hours of chemotherapy completion. Of 50 cases studied, none showed ECG changes as immediate or delayed side effect.

Discussion:

The results of this study showed that, single 0.25 mg dose of palonosetron given intravenously at the start of chemotherapy significantly reduces the chemotherapy induced nausea and vomiting.

Only 2 out of 50 patients had vomiting 24 hours post chemotherapy completion(delayed CINV) whereas none of the patients had nausea 24 hours post chemotherapy (delayed CINV) thus proving that the efficacy of palonosetron is more for delayed CINV than for acute CINV. Two patients who had vomiting after 24 hours of post chemotherapy, repeat dose of 0.25 mg of palonosetron was given. The results were comparable with similar study done by Luigi Celio, Monica Niger et al.[5] Also, in this study, none of the patients had ECG changes, which suggests that palonosetron can be used safely in patients undergoing chemotherapy.

Palonosetron has been recommended in the international guidelines for the prevention of CINV. The high safety profile and the opportunity to reduce the total corticosteroid dose with no loss in efficacy of chemotherapeutic drugs against delayed CINV indicates the safety and efficacy of Palonosetron.

Conclusion:

0.25 mg single dose of palonosetron given intravenously was thus found to be an effective agent in the prevention of CINV with efficacy more for delayed CINV than acute CINV.

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